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# DEVELOPING REGULATIONS FOR RESEARCH INVOLVING ADULTS WHO LACK DECISION-MAKING CAPACITY

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The use of human subjects in clinical research has played an essential role in understanding illness and in determining optimal treatment of disease. For over thirty years, scientists, clinicians and the public have debated the appropriate regulatory balance between protection of research subjects from the risks of research and the acquisition of important scientific knowledge (1). Recent reports concerning research involving subjects with cognitive impairment caused by mental illness have brought into question the adequacy of the rules for the protection of vulnerable research subjects with diminished mental functioning (1,2). A study at the University of California, Los Angeles, which included withdrawal of medication from patients with recent-onset schizophrenia was found after review by the Office for Protection from Research Risk of the U.S. Department of Health and Human Services to have deficiencies in obtaining informed consent and in the institutional processes for protecting vulnerable research subjects (2). Litigation in New York initiated by patients in mental health facilities who were concerned about the consent procedures for research participation invalidated portions of the research regulations promulgated by the state Office of Mental Health to protect the subjects of research in publicly funded psychiatric facilities (3).

These public allegations of research misconduct have resulted in several state groups as well as the National Bioethics Advisory Commission, at the request of the President of the United States, advocating new regulations to protect vulnerable research subjects who lack decision-making capacity. An analysis of the background of these discussions and the extant recommendations may be helpful to clinicians, researchers, and the public in deciding what, if any, changes are needed in national research regulations to protect the subjects of research.

Modern discussion about the ethics of research began with the Nazi doctors' trial at the close of World War II. In response to atrocities carried out on concentration camp inmates in the guise of medical

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research, American judges at the military tribunal in Nuremberg created the first guidelines for the protection of the human subjects of medical research (4). An essential component of this "Nuremberg Code" is that: *the voluntary consent of the human subject is absolutely essential.* If taken literally, as was intended, this would preclude research on any adult or child incapable of full and complete decisional capacity. The Code expounded on the meaning of voluntary consent:

> *This means that the person involved should have the legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.*

American academics generally agreed in principle but ignored this first code of research ethics, until 1966, when an article by Henry Beecher published in the New England Journal of Medicine entitled, *Ethics and Clinical Research,* alerted the research community and the American public to potential problems in research studies utilizing human subjects (5). Beecher analyzed 22 recently published studies and questioned whether clinical researchers were adequately informing subjects of the risks of experiments and obtaining voluntary and informed consent. On the heels of this indictment of the medical research enterprise came the revelation in 1972 that a government-funded study (often called the Tuskegee syphilis study) initiated in 1932 to examine the natural history of syphilis had not offered penicillin treatment to the research subjects even though antibiotic therapy had become standard treatment for syphilis in the 1940s (6).

In response to these and other allegations about the conduct of clinical research, in 1974, the U.S. Congress created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission set out to answer several important questions, including: *What principles should guide human*

*subjects research?* and, *Is it unethical to conduct non-therapeutic research on individuals who cannot consent?* The Commission outlined the framework for the protection of human subjects of research in the *Belmont Report* published in 1979 (7), and defined three principles which form the ethical basis of human subjects research: *respect for persons, non-maleficence, and distributive justice.* The principle of respect for persons is most relevant to discussion of research with incapacitated patients in that it encompasses two important aspects: first, investigators should demonstrate respect for individual research subjects by treating them as autonomous persons and respecting their right to voluntarily consent to or refuse participation; second, children and adults with diminished autonomy are entitled to increased protection.

The National Commission, in contrast to the authors of the Nuremberg Code, supported research studies involving incapacitated patients under specific circumstances and with specific safeguards in order to allow the development of new knowledge regarding mental illness, neurological disorders, and diseases affecting children. Within five years the Commission published nine reports with detailed recommendations for regulatory action concerning research on all human subjects including the special cases of fetuses, prisoners, children, and the institutionalized mentally ill. By 1983, the Department of Health, Education, and Welfare had issued regulations covering all federally funded research, including special rules concerning studies of pregnant women, prisoners, and children (8). However, the Commission's additional specific recommendations concerning adult persons with diminished capacity to consent to research because of a mental disability were never promulgated as regulations (9). The debate at that time was no different from the arguments today and revolved around the concerns of clinical research scientists that the proposed rules and safeguards would impede critical advances in the understanding of the brain, and the arguments set forth by patients' rights advocates were that mentally ill subjects were vulnerable to abuse, particularly those who were hospitalized and estranged from their families.

Although there have never been specific regulations governing research subjects with mental illness, developmental disabilities, dementia, and other neurologic disorders associated with inability to provide informed consent, federal law has created local Institutional Review Boards (IRBs) which are expected: a) to ensure that research occurs only with the consent of the subject or the subject's legally authorized representative, b) to be particularly cognizant of the special problems of research involving vulnerable populations including men-

tally disabled persons, and c) to adopt additional safeguards as necessary to assure the rights and welfare of such subjects (8).

Many unanswered questions remain concerning IRB processes and procedures and the consistency and adequacy of individual IRBs in relationship to protecting the interests of cognitively impaired adults. Many critics believe that research on cognitively impaired patients may be essential to understanding of disorders ranging from Alzheimer's disease to schizophrenia and stroke, but they argue that the bulk of research should be carried out with capacitated patients. When research with incapacitated patients is absolutely necessary, they believe there ought to be uniform national safeguards to assure adequate protection of mentally disabled persons as well as standards to determine the characteristics of a research study or a proposed population that would require such additional safeguards concerning the consent process and the implementation of the research (10–12).

In order to allow research to be conducted with subjects unable to provide voluntary and informed consent, IRBs have permitted surrogate decision-making. In the realm of clinical care and treatment, decisions by surrogates on behalf of persons incapable of autonomous choice have become common practice, including surrogate refusal of life-sustaining treatment with the resultant death of the patient (13). In these situations, the surrogate is obligated to provide a substituted judgment for the patient by considering the views and values expressed by the patient when capable. If the patient's choice is unknown and cannot be inferred from prior statements or actions, the surrogate is asked to choose that course of action which is consistent with the best interests of the patient (14). To promote respect for a patient's former autonomous wishes in the clinical setting, advance directives have been used such as a living will which states the patient's general beliefs about desired treatment options under certain circumstances, or a health care proxy which endows a person with the legal authority for health care decision-making if the patient becomes incapacitated.

Research differs from clinical care in several important ways that potentially call into question the applicability of the standard surrogate decision-making model. Research may not offer the prospect of direct benefit to the individual research subject. Although clinical research should always be intended to enhance knowledge and thus benefit future members of our society, it may or may not benefit the subjects. Even when the intent of the research is to potentially provide therapeutic benefit to the patients, the nature of research includes uncertainty as to possible benefits and harms and, therefore, precludes knowing what is "best" for the individual subject. People who partici-

pate in research studies are referred to as "subjects" and those who receive clinical care and treatment are called "patients". This semantic distinction is far more significant than is often appreciated by physicians and patients alike. Patients have the right to expect that doctors will place the interests of the individual who is sick as their primary concern, and patients ought to feel protected by the covenant inherent in the doctor-patient relationship. Research subjects, on the other hand, ought not believe that the primary or sole concern of the clinical research scientist is the health and well being of the subjects of the research. Research scientists are additionally motivated by the search for knowledge and the interests of future patients and the society at large.

The federal regulations governing research in children have recognized the special role of the surrogate, in this case the parent, in giving permission for children to be enrolled in research studies (15). Children are thought to be particularly vulnerable as research subjects because they are rarely competent to provide voluntary and informed consent and have historically been subjected to abuse by researchers (16). Parents are viewed in our society as the legal guardians and natural surrogates of children and have broad authority to make decisions for them. Parents are obligated to meet societal standards of adequacy in regard to such critical decisions as food, shelter, and medical care for their children. Parents are given broad discretion but not complete authority, in the clinical context and the research setting, to determine what risks are acceptable for their children. Although autonomous adults may consent to research which has considerable risk and no potential for direct benefit, such as a heart catheterization in a normal volunteer to test the efficacy of a new drug, federal regulations preclude such research in healthy children even if the parent might give permission.

The federal regulations classify research with children into four categories (15). First, research is permitted if it entails no greater than "minimal risk" as long as the permission of a parent and the "assent" of the child, if developmentally appropriate, is obtained. The regulations define *minimal risk* to mean:

> *that the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.*

Second, research is permitted that involves greater than minimal risk if it presents the prospect of direct benefit to the individual

research subject. Such research must be determined by the IRB to have the risks justified by the anticipated benefits, and to always include the permission of a parent or guardian, and the assent of the child, when appropriate.

The third category of research is more controversial. An IRB is permitted to approve research involving greater than minimal risk and no prospect of direct benefit to individual children if it is likely to yield generalizable knowledge of "vital importance" about the subject's disorder or condition; the study represents only a "minor increase over minimal risk"; the interventions are "reasonably commensurate" with those inherent in the actual medical, social, and educational lives of the subjects; the child assents, if appropriate; and both parents, if available, give permission.

There is even a fourth category of permissible research in children which involves significant risk to the subjects but "presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children." Such research may not be approved by a local IRB but is permitted only after a national review and the approval by the Secretary of Health and Human Services. This category has rarely been pursued by clinical researchers but remains open as an option in extraordinary circumstances.

Definitions in the child regulations have met with significant criticism. The definition of "minimal risk" has been viewed as imprecise and subject to broad interpretation (17). Children vary in the level of risk encountered in their daily lives based on many social considerations. A technical reading of the definition might subject some children to inordinate risks based on the unfortunate circumstances of where and how they live. Fairness would dictate that the definition of minimal risk be that level of risk inherent in the lives of normal, average persons, but the present regulations are thought by some not to be explicit enough to assure standard and uniform implementation by all IRBs.

The third category of permissible research for children which includes the concept of a minor increase over minimal risk is considered even more problematic. This category is criticized because it uses those experiences encountered in the everyday lives of children affected by illness as the reference point for a level of permissible risk with no compensating benefit. Some commentators consider this standard perverse because already sick children are allowed to be subjected to more pain and discomfort than healthy children (18). However, others argue that this category of research is essential for investigating the underlying pathophysiology of disorders that impact on children without placing those children at undue risk. In addition, clinicians argue that

patients experiencing a chronic illness and its routine diagnostic tests and procedures are likely to be less anxious and frightened and more accepting of such interventions than healthy subjects. Most clinicians and investigators consider diagnostic tests such as PET scans or MRIs as entailing minimal risk, but such procedures do not fit the regulatory definition of minimal risk. They represent examples of procedures which are permissible in the third category of research, minor increase over minimal risk. Thus, in the absence of therapeutic intent, these tests which are used frequently to increase the basic understanding of disorders of the brain, would not be able to be performed, were it not for the existence of the concept of a minor increment over minimal risk.

Conceptually, in order to permit research with no therapeutic intent and a minor increase over minimal risk, the investigators, the IRB, and the parents or guardian are each expected to assess the research proposal. They must determine whether the study is designed to obtain generalizable knowledge of vital importance to patients with a specific disorder, and evaluate the level of risk to determine that it is only a minor increment over the risks of everyday life and commensurate with the prior experiences of the patients who will be subjects. This process is fraught with the possibility of abuse even though it has been used over the past twenty years by IRBs throughout the country with what appears to be reasonable success in protecting the interests of the vast majority of research subjects.

In fact, there have been reports of alleged abuse of incapacitated research subjects enrolled in approved studies. These allegations question the IRB assessment of the level of risk and raise concern about whether surrogates ought to be allowed to consent to research studies with no direct therapeutic intent and any risk which is more than minimal. In response to these concerns, the American College of Physicians developed a position paper on cognitively impaired adults as research subjects, published in 1989 (19). Cognizant of the distinctions between research and clinical care, aware of the importance of research with patients of diminished capacity, and concerned with the potential for misinterpretation of the definitions within the child regulations, the College created guidelines which aim to allow progress in research while upholding the rights and protecting the welfare of potential experimental subjects. The College concluded:

—*Consent to participate in research can, at times, be obtained in advance from the subject, before he or she becomes incompetent.*
—*Where there is no advance directive, a legally authorized representative should act as the surrogate decision maker for an incompetent potential subject.*

—*Surrogates may consent to therapeutic research if participation is in the incompetent person's best interest, that is, if the net additional risk caused by participation is small, and there is scientific evidence that participation is reasonably likely to offer benefits over standard treatment or no treatment, if none exists.*

—*Surrogates should not consent to non-therapeutic research that presents more than a minimal risk of harm or discomfort.*

—*Special protections are necessary for chronically institutionalized subjects.*

These guidelines, if adopted, would decrease the potential for abuse of incapacitated research subjects, but would also preclude a large number of studies presently approved by local IRBs. The authors of the guidelines understand that such restrictions may impede the research process but accept the admonition of the philosopher Hans Jonas, that society will ultimately be diminished more by a loss of the rights of research subjects and the lack of adequate protection of their interests than by the potential slowing of scientific inquiry (20). The guidelines invoke the concept of an advance directive for research participation executed before the research subject has lost capacity and implemented under the supervision of the surrogate. Unless there exists a research advance directive, these recommendations preclude all non-therapeutic research with greater than minimal risk. In addition, the guidelines even prohibit greater than minimal risk research with the potential for direct benefit unless the researcher offers prior evidence of likely greater benefits and no substantially greater risks than standard treatment.

The recently created National Bioethics Advisory Commission is also in the process of developing recommendations for research with incapacitated adults. A draft document entitled *Research Involving Persons with Mental Disorders that May Affect Decisionmaking Capacity* is presently being circulated for public comment and final action by the Commission (21). The Commission has concluded that there is a need for new federal regulations to standardize IRB processes and procedures and to assist IRBs in defining acceptable levels of risk and special protections for research involving incapacitated adults. The Commission's draft document includes the following requirements for research with persons with mental disorders:

—*A conscious person who has been determined to lack capacity to consent to participate in a research protocol must be notified of that determination before permission to participate can be sought from his or her legally authorized representative; if permission to enroll is*

*given, the subject must be notified of that decision.*

—*Any apparent dissent by a subject from participation in research at any time must be honored.*

—*Investigators must justify their determination of the level of risk entailed by the research protocol and describe the special informed consent procedures and other protections developed in light of the level of risk posed by that particular protocol.*

—*For subjects who have been determined to be incapable of making a decision about participation:*

  —*minimal risk research is permitted with the advance directive of the subject or the informed permission of a surrogate;*

  —*greater than minimal risk research which offers the prospect of direct benefit to the subject is permitted with the specific advance directive for research executed by the subject or with the informed permission of the subject's legally authorized representative.*

  —*greater than minimal risk research that does not offer the prospect of direct benefit to the subject is permitted with the specific advance directive for such research executed by the subject and the concurrence of the research proxy appointed in the research advance directive.*

—*Controversial study designs such as those to provoke symptoms, withdraw medications, or which contain a randomization into a placebo group must be justified by the investigators and additional safeguards such as an independent physician advisor considered in such cases.*

The Commission's draft recommendations concur with those of the American College of Physicians and create only two categories of research risk: minimal and greater than minimal. This categorization precludes surrogate consent for research with no prospect of direct benefit and more than minimal risk unless there exists a specific advance directive consenting to this type of research. The rationale for this view is clear: only autonomous adults ought to be empowered to make the altruistic decision to place themselves at risk solely for the benefit of others. An autonomous adult may signal an interest in becoming a subject of research, if and when he or she loses capacity, by creating an advance directive and designating a surrogate who will make the specific decision contemporaneously. The use of an advance directive respects individual autonomy and may decrease the potential for abuse of incapacitated research subjects. However, it is likely that reliance on this approach will significantly decrease the number of incapacitated subjects eligible to be enrolled in research projects which offer no prospect of direct benefit.

Within the research community, there is great concern about the likelihood of patients creating an advance directive for research while capacitated. Some commentators have advocated a national program to encourage the creation of advance directives for research by patients with illnesses likely to result in the loss of capacity, but similar programs for the creation of advance directives for clinical care and treatment have met with only modest success even though of far greater import (13). In addition, many incapacitated patients who would be subjects of research studies lose capacity suddenly and would not have even considered an advance directive for future research studies.

In the summer of 1998, the National Bioethics Commission received 87 public comments concerning its draft recommendations. A major criticism of the Commission's document was concern about a system which precludes many research studies presently permissible under federal regulation and places research that entails risk only slightly greater than minimal in the same category and with the same stipulations as research with highly invasive and risky components. In contrast to the Commission's recommendations, two state groups, the New York State Department of Health Task Force (22), and the Maryland Attorney General's Research Working Group (23), have concluded that for research involving incapacitated adults, there would be benefit to maintaining for adults the categories of permissible research developed to regulate research on children. This approach would permit surrogate decision-making for research studies with no prospect of direct benefit to individual subjects and a level of risk which is a minor increase over minimal. The rationale of the state groups is fivefold: that execution of many advance directives for research participation is unlikely, that the testimony by patients and advocacy groups indicates a strong desire to understand better the basic etiology and pathogenesis of mental disorders, that it is possible to explicitly give examples of those types of procedures which would constitute a minor increment over minimal risk, that additional safeguards to assure uncoerced and informed surrogate decision-making can be developed, and perhaps most importantly, that regulations developed for the protection of children have for the most part been successful.

In the final analysis, it appears important and timely to develop specific national guidelines for IRBs to use in the assessment and implementation of research protocols which include adults who lack decision-making capacity. The challenge is to create a system that allows important clinical research in order to provide insight into the basic understanding and treatment of diseases that impair central

nervous system functioning, while assuring that vulnerable people are treated with respect and protected from abuse. Advance directives for research as one method to encourage respect for the autonomous wishes of formerly capacitated patients is laudable, but is unlikely to be useful in more than a small percent of the potential subjects of research. Thus, the task remains to determine at what levels of risk in research studies without compensating benefit should surrogates be permitted to provide consent for incapacitated adults and what additional safeguards should be required to assure uncoerced decision-making and ongoing protection of the individual subjects during the research study.

To address the first question of what level of risk ought to be permissible without compensating benefit, we might turn to a reasonable-person standard. Since all actions have some level of risk, permissible risk with no compensating benefit ought to be at a level of harm or discomfort that a reasonable person would consider sufficiently trivial as to be acceptable for the benefit that might accrue to others in the future. I believe that the present definitions of minimal risk and a minor increase over minimal risk convey this concept. What is needed is nationally agreed-upon examples of procedures which ought to be included in each of these risk categories and the relevant characteristics of these procedures in order to give guidance to IRBs. This would deal with the problem of variation among IRBs in interpreting the present definitions of acceptable risk levels. After defining the permissible levels of risk and giving examples, regulations must also assure that surrogates make uncoerced choices which reflect the values of the subject and are in the subject's interests.

The role of the surrogate is to assess, in the case of a formerly capacitated patient, whether the subject would wish to participate in this specific research project, and would accept this level of risk either for the potential personal benefit or for the good of others regardless of personal benefit. In the case of those whose wishes are not known or unknowable, the surrogate must decide what is in the interests of the subject. Can any level of risk for no potential of benefit be in the interests of an incapacitated patient? I would argue that when there is only a small risk of harm or discomfort, it can be in a patient's interests to participate in a research study even if there is no potential for direct benefit. Benefit can accrue from the fact that the research might benefit other present or future family members of the subject, that many sick people feel some desire or obligation to help others similarly afflicted, and that some individuals hold the communitarian notion of a shared interest in bettering our collective futures.

Some critics are unwilling to trust that surrogates will make these judgments in the interests of patients. Yet, it seems broadly paternalistic to impugn the integrity of surrogates and to be overly concerned about their ability to make reasoned choices in the interests of their loved ones. Moreover, several groups have identified safeguards that could be used when surrogates are being asked to make difficult decisions for incapacitated adults. Such safeguards could include independent monitors of the consent process and research advisors who could assist surrogates in understanding the risks and benefits of research protocols. This approach, the utilization by IRBs of specific safeguards commensurate to the risks of the research, could be an effective way of protecting vulnerable subjects while still allowing surrogate decision-making.

The regulations being developed for research with incapacitated adults should build on the regulations for research in children, clarify the present definitions of minimal risk and a minor increment over minimal risk by giving explicit examples of risks and discomforts which fit into these categories, and propose additional safeguards such as independent consent monitors and advisors which should be imposed by IRBs based on the level of risk of the proposed research. This approach will protect future vulnerable subjects while still allowing important research to be conducted.

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## DISCUSSION

**Butler,** Houston: I'd like to ask one question that relates to the fact that most of the studies you showed there are governmentally driven. To what extent have the professional societies stepped forward to really address these issues? You have mentioned one, The American College of Physicians, but it seems to me that our societies ought to be more proactive.

**Fleischman:** I think that is a very important comment and I share your view. The research societies, both in the adult world and in the pediatric world, have a serious stake not only in protecting the research enterprise, but in creating appropriate regulations of research so that the subjects are protected.

**Hendrix,** Baltimore: Thank you very much for this nice summary of the problems that face a study of people who are not able to make full decisions. In Maryland the action taken by the Attorney General, and others, was actually started by inquiries from our institutional review board and particularly by Marshall Folstein, who was on our faculty at that time. Based on the criteria that we have for giving therapy in patients who cannot make decisions for themselves, a similar approach to consent has worked very well over the years. I agree with you that having people give advanced directives

sounds legally nice and simple, but you can't give a directive that is truly informed if you don't know what the studies are going to be in the future.

**Fleischman:** One of the great problems, however, is in those studies that are not therapeutic in their intent. When we are faced with trying to define the pathophysiology of Alzheimer's disease, or some of the issues around schizophrenia research, it is a much more complicated analysis to merely allow surrogates to make decisions the way we would in a therapeutic transaction. Inherently the therapeutic transaction involves a recommendation from the physician and a permission given by the surrogate. In the non-beneficial research context, we really have what has been called in ethics literature, "clinical equipoise". We really don't know whether there is going to be benefit or not and some suggest that surrogates ought not have the right to make those choices. As you know, I would disagree.

**Dale,** Seattle: Could you discuss the termination of clinical trials? How do you design a study that you think may require 100 or 1000 people, but you believe you should stop as soon as you have shown benefit, or unlikely to show benefit.

**Fleischman:** Well, that is a very important clinical research question and there has been a great deal written on the ethics of the last patient enrolled in a randomized clinical trial. We have fairly sophisticated data-analytic skills now in that most large research studies will have points along the way to review the results and many multi-center studies have data-safety and monitoring boards. I think we are going to move more and more that direction because of the ethics of continuing clinical trials after efficacy has been shown. We have seen an increasing number of studies being stopped for success. I think this is a tribute to the data-safety and monitoring approaches and good statistical analytical approaches.

**Ross,** Baltimore: You mentioned the problems in the mentally ill and with children. Have you given any thought to the emergency situation? I've been involved with a little company which produces an inflatable vest to give closed chest massage. This device could save a lot of lives it if were generally available, but the problems of obtaining approval are so great that the device is not yet available. The device is for use in the emergency situation in patients who may be unconscious and may not be able to give permission. I wonder if you have any thoughts on that?

**Fleischman:** Actually, for good or for bad, the federal regulations have now addressed that group of patients. It is possible for emergency medicine physicians to come forward with protocols to their IRB's and there is consent presumed as the subjects come to the Emergency Room unconscious. It is a very narrow window; the trial has to be therapeutic in its intent and the community has to be involved in the discussion of the trial, but there actually is now a federal regulatory structure which will allow for so-called emergency consent procedures in research.

**Hornick,** Orlando: I was going to ask the same question because we have been faced with that in our trauma center with a brain-damaged individual and some of the new therapeutic approaches to try to preserve brain function. We have been concerned about the delayed consent that needs to be obtained in those people. You have just addressed it in your comments about Doctor Ross' concern, but this is something that our IRC has discussed at length and many members feel uncomfortable with this process.

**Fleischman:** The field of emergency medicine is moving very rapidly and many acute interventions are most critical in the first hours. It is critical to be able to do research on this population of unconscious patients. The federal regulations will need some fine tuning over time. The investigators are having a lot of problems with these new regulations. They are rather stringent, they are difficult, and this question of community consultation is an interesting one nationally. How do you consult with a community? What does it constitute? Is it the community around your hospital, is it a broader

community, is it a community of likely subjects of the research? What does consultation really mean? Often times when the large academic medical center goes out into the community to ask for consultation, what they really get is advocacy for health care delivery. Often times the community, rightly so, wishes a quid pro quo for their consent to allow this research project. The researcher has nothing to do with creating a primary care clinic on the corner or enhancing emergency care for some community group. That is what ends up happening and that is what we have been hearing around the country. This has been a significant problem.

**Prout,** Boston: The situation in regard to surrogates is analogous to the Health Care Proxy. The studies which are going to be made in mental institutions, chronic disease institutions, and prisons, are in places difficult to access. We don't know the biases of these surrogates. All systems, of course, are subject to the frailty of human nature, so I think the selection of the right people as surrogates, and their supervision, is extremely important.

**Fleischman:** I think that is a very important point. In the reports of both the Maryland and New York groups, procedural safeguards have been suggested instituting things that are called independent consent monitors and research advisors who would be able to counsel surrogates independent of the research team. These, I think, are critical safeguards and, of course, many of the people who have criticized clinical research in mental institutions have said that the surrogates really have separated from those patients and don't advocate for the interests of those patients even if they are relatives. It is important for us to create procedural safeguards to assure that the surrogates are reflecting the interests of the patients.

**Hendrix,** Baltimore: You say that the federal regulations do allow the conduct of investigation in individuals who cannot give consent in an emergency situation. Unfortunately, these regulations just really can't be activated because to get a community to understand and accept them has been found an impossibility in our experience.

**Fleischman:** I share your concern. They have been activated, though, in some institutions around the country. Some have tried to go out to the community and have used the newspapers, have used community liaisons with the churches and senior groups, etc., but it is actually being studied now. IRB chairs are studying the issue of what does it mean to go to the community. I think that conceptually it was a nice idea, the idea to ask the community from which the subjects would come to at least accept the general idea of the research, but in reality it is a very difficult, if not impossible task.

**Ross,** Baltimore: A follow up on my previous question: I know about the "emergency consent procedures" but consider them to be exceedingly difficult to implement. The problem has to do with obtaining community consent. For example, a hospital in California was ready to go with a study and had placed the required notice in the newspaper in English and Spanish, but they were rejected because there was no notice in Chinese. The regulations and their interpretation are making progress impossible.

**Fleischman:** I think the regulations don't require that level of specificity, but obviously there are people interpreting this concept of community consultation in various ways.

**Ross:** I think what we are facing is the challenge of increasing regulatory authority and the impact on clinical investigation. Obviously this is something our society should be very concerned about.